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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,497	10/30/2003	Stephen C. Suffin	CNSR-07141	8061

7590 01/23/2007

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EXAMINER	
KIM, JENNIFER M	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/697,497	SUFFIN ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *4-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed October 23, 2006 have been received and entered into the application.

Action Summary

The rejection of claims 1-3 under 35 U.S.C. 112, second paragraph is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 1-3 under 35 U.S.C. 103(a) as being unpatentable over Quessy et al. (US 2002/0147196 A1) of record further in view of Zakrzewska et al. (#84, PTO-1449), (Journal of Neurology, Neurosurgery, and Psychiatry 1989) of record is being maintained for the reasons stated in the previous Office Action.

Response to Arguments

Applicants' arguments filed October 23, 2006 have been fully considered but they are not persuasive. Applicants argue that there is no motivation to combine the teachings of Quessy et al. and Zakrzewska et al. This is not persuasive because the strongest rationale for combining references is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would

have been produced by their combination. In this case, Zakrzewska et al. teaches the motivation to modify the illustrated composition taught by Quessy et al. to select oxcarbazepine because oxcarbazepine not only possesses anti-neuralgic properties for managing intractable trigeminal neuralgia but also elicits excellent therapeutic response in controlling pain. Further, Zakrzewska et al. teach that oxcarbazepine have advantages because it has no side effects. Therefore, one of ordinary skill in the art would have been motivated to formulate bupropion with oxcarbazepine in order to successfully treat neuropathic pain without the side effects. There is a reasonable expectation of successfully treating neuropathic pain without side effects with a combination of bupropion and oxcarbazepine because oxcarbazepine is well taught by Zakrzewska et al. having excellent therapeutic response in controlling pain without side effects. Applicants argue that Quessy et al. and Zakrzewska et al. do not teach all the claimed elements because Quessy et al. does not teach a composition comprising a combination of oxcarbazepine and bupropion and only briefly mentions oxcarbazepine as a sodium channel blocker. This is not persuasive because Quessy et al. selected lamotrigine rather than oxcarbazepine as their illustration does not mean it does not teach all the claimed elements required in the present invention. Quessy et al. is not **limited** to working examples but also for what one of ordinary skill might reasonably infer form the teaching. In this case, Quessy et al. illustrate a pharmaceutical composition bupropion and sodium channel blockers including oxycarbazepine and lamotrigine useful for the treatment of neuropathic pain, while in the secondary reference, Zakrzewaska et al. teach the advantages and benefits/effects of

oxcarbazepine for the very same treatment. Accordingly, it is *prima facie* obvious to modify the composition of Quessy et al. by replacing lamotrigine with oxcarbazepine because oxcarbazepine lacks side effect and because Quessy et al. teach that bupropion can be formulated with any one of disclosed sodium channel blockers including oxcarbazepine or lamotrigine which are equivalents both having the anti-neuralgic properties for treating neuropathic pain in combination with bupropion. Applicants argue that Quessy et al. and Zakrzewska et al. do not teach a reasonable expectation of success because the apparent requirement of chemical compound for bupropion/oxcarbazepine was not discussed in Quessy et al. This is not persuasive because the burden of proof is upon applicants to show that instantly claimed subject matter is different and unobvious over those taught by prior art. See *In re Brown, 173* USPQ *685, 688; In re Best, 195* USPQ *430 and In re Marosi, 218* USPQ *289, 293.* In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claimed would have been obvious within the meaning of 35 U.S.C. 103. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

In view of the above Office Action of July 20, 2006 is deemed proper and asserted with full force and repeated herein to obviate applicants' claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quessy et al. (US 2002/0147196 A1) of record further in view of Zakrzewska et al. (#84, PTO-1449), (Journal of Neurology, Neurosurgery, and Psychiatry 1989) of record.

Quessy et al. teach a pharmaceutical composition comprising **bupropion** and sodium channel blockers including **oxcarbazepine and lamotrigine** useful for the treatment of **neuropathic pain**. (page 5, claims 1-3). Quessy et al. illustrate the composition comprising **bupropion and lamotrigine** (page 5, Example 3, claim 6). Quessy et al. teach that using the test compound lamotrigine in a pre-clinical experiment, no adverse side effects were observed. ([0038]). Quessy et al. also teach that the composition can be formulated with **mixtures of NE-reuptake inhibitors which exert analgesic activity (analgesics)**. (page 1, [0009], [0010]). Quessy et al. further teach that the composition can be formulated as a **transdermal patch, sterile injectable solution, tablet, capsules, oral liquid** or **a sterile liquid for injection** and can be formulated with suitable **polymeric** materials. ([0021]-[0027]). Quessy et al. additionally teach that the composition manifests **synergism** in the treatment of neuropathic pain ([0009]). Quessy et al. lastly teach that there is a need for a pharmaceutical composition that can alleviate neuropathic pain or/its symptoms effectively. (page 1, [0004], [0007]).

However, Quessy et al.'s illustrated composition (example 3) uses lamotrigine with bupropion, rather than oxcarbazepine as instantly claimed.

Zakrzewska et al. teach that **oxcarbazepine** possesses **antineuralgic properties,** is effective in the management of intractable **trigeminal neuralgia,** and

elicits an **excellent** therapeutic response in **controlling pain without side effects**. (abstract).

It would have been obvious to one of ordinary skill in the art to modify the composition of Quessy et al. by replacing lamotrigine with oxcarbazepine, because Quessy et al. teach that bupropion can be formulated with any one of disclosed sodium channel blockers including oxcarbazepine or lamotrigine, and because Quessy et al. teach that oxcarbazepine and lamotrigine are equivalents both having the anti-neuralgic properties for treating neuropathic pain in combination with bupropion. Further, Zakrzewska et al. also teach that oxcarbazepine has no side effects. One of ordinary skill in the art would be motivated to make such a modification with oxcarbazepine in order to fulfill the need of a pharmaceutical composition and providing variety for the treatment of neuropathic pain, not only possessing anti-neuralgic properties but also lacking side-effects as taught by Zakrzewska et al. There is a reasonable expectation of successfully treating neuropathic pain without side effects with a combination of bupropion and oxcarbazepine, the latter well taught by Zakrzewska et al. as possessing excellent anti-neuralgic properties with an excellent therapeutic response in controlling pain. With regard to further combining with a third drug as set forth in claim 2 and the specified formulation as set forth in claim 3, all deemed obvious because Quessy et al. teach that NE-reuptake inhibitors exert analgesic activity (analgesics) and, therefore, can be incorporated in the obvious combination and because the various formulations set forth in claim 3 are taught by Quessy et al. as suitable formulations for the obvious combination. One would have been motivated to further incorporate analgesics in a

mixture to the combination in various formulations disclosed by Quessy et al. in order to successfully formulate an ultimate regimen for the treatment of neuropathic pain possessing at least one synergistic effect disclosed by Quessy et al. without a side effect. Absent any evidence to contrary, there would have been a reasonable expectation of successfully improving the anti-neuropathic pain composition of Quessy et al. by combining bupropion and oxcarbazepine in order to fulfill the need of a pharmaceutical composition that can alleviate neuropathic pain without as a side effect.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

THIS ACTION IS MADE FINAL. Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sreenivasan Padmanabhan
Supervisory Primary Examiner
Art Unit 1617

Jmk
January 8, 2007